UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,838	12/22/2005	Hideki Kubota	281748US0PCT	2991

22850 7590 06/08/2010

OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, L.L.P.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
OH, TAYLOR V	

ART UNIT	PAPER NUMBER
1625	

NOTIFICATION DATE	DELIVERY MODE
06/08/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

Office Action Summary	Application No.	Applicant(s)	
	10/561,838	KUBOTA ET AL.	
	Examiner	Art Unit	
	Taylor Victor Oh	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 March 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,8-17 and 21-23* is/are pending in the application.

4a) Of the above claim(s) *21 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 8-17* is/are rejected.

7)☒ Claim(s) *23* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *4/1/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

In spite of adding some additional limitations to the claims in the amendment filed on 3/12/10, there are still some issues to be addressed and resolved; the examiner has decided to withdraw the previous Office Action and the application is subjected to another Non-final rejection .

The Status of Claims :

Claims 1, 8-17, and 21-23 are pending.

Claims 1, and 8-17 are rejected.

Claims 21-22 are withdrawn from consideration.

Claim 23 is objected

DETAILED ACTION

1. Claims 1, 8-17, and 23 are under consideration in this Office Action.

Priority

2. It is noted that this application is a 371 of PCT/JP04/09132 (06/29/2004), which has a foreign documents: Japan 2003-187796(06/30/03) and Japan 2004-099151(06/30/03).

Drawings

3. None.

Claim Objections

Claim 23 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Although the specification merely mentions that the present invention relates to a medicament to treat various diseases caused by abnormal production or secretion of beta-amyloid protein such as Alzheimer disease or Down syndrome, the specification falls short because data essential for treating as Alzheimer disease or Down syndrome by means of administering the composition containing the formula(I) is not described in the specification.

First, the instant claims cover the treatment of a disease such as Down syndrome, for which there is no enablement provided.

For a compound or genus to be effective against Down syndrome is contrary to the findings of medical science.

Down syndrome is a well-known genetic condition in which a person has 47 chromosomes instead of the usual 46. In most cases, Down syndrome occurs when there is an extra copy of chromosome 21. This form of Down syndrome is called Trisomy 21. The extra chromosome causes problems with the way the body and brain develop. Down syndrome is the most common single cause of human birth defects. Many different medical conditions are seen in babies born with Down syndrome, including:

- Birth defects involving the heart, such as an atrial septal defect or ventricular septal defect
- Dementia, Alzheimer's type may be seen
- Eye problems, such as cataracts (most children with Down syndrome need glasses)
- Early and massive vomiting, which may be a sign of a gastrointestinal blockage, such as esophageal atresia and duodenal atresia
- Hearing problems, probably caused by regular ear infections
- Hip problems and risk of dislocation
- Long-term (chronic) constipation problems
- Sleep apnea (because the mouth, throat, and airway are narrowed in children with Down syndrome)
- Teeth that appear later than normal and in a location that may cause problems with chewing

- Underactive thyroid (hypothyroidism) .

Regarding its treatment, there is no specific treatment for Down syndrome. A child born with a gastrointestinal blockage may need major surgery immediately after birth. Certain heart defects may also require surgery.

Not only the treatment of Down syndrome is unknown in the medical field, but also, the method for the possible treatment of a beta-Amyloid protein-associated disease called Alzheimer's Disease (AD) is doubtful.

Many scientists and medical doctors are in search for finding the main causative factors in order to treat the Alzheimer's Disease. For example, according to Meda et al (Nature 374,647 (1995) and Larner (Neurosci. Res. Commun. 20 , 147 (1997), β-amyloid peptide was shown to exert direct toxic effects on neutrons and to inhibit neurite growth in vitro. Thus, therapeutic approaches that can modulate βA peptide toxicity have been hypothesized to represent important methods for controlling the onset of AD. It is postulated that if neuronal cells can be protected from βA peptide/senile plaque-induced toxicity, the onset of AD may be delayed ; furthermore, St. George-Hyslop et al (Nature 400, 116 (1999) indicates that an anti-βA protein antiboby was shown to clear senile plaques and protect mutant PDAPP mice from the onset of AD. From this, the generation of reactive oxygen intermediates through oxidative stress caused by βA peptide has been suggested to be the major pathway of βA peptide-induced cytotoxicity. Thus, there is no positive correlation between the βA peptide-induced toxicity against certain cells and the treatment as claimed.

So far, they do not know for sure what caused people to have the AD. The induced beta-Amyloid protein toxicity is one of the outcomes of the AD, but not the underlying cause of the AD.

Furthermore, in the specification, there are no examples for treatment of Down syndrome or Alzheimer disease as well as their corresponding pharmacological data except the data (table 1)(page 554) related to the inhibitory activity against the production or secretion of beta-Amyloid protein are insufficient to be used as the treatment-data for the AD. Therefore, the specification falls short because data essential for treating Alzheimer's Disease whether the AD is induced by the beta-Amyloid protein or not are not described in the specification.

The nature of pharmaceutical arts is that it involves screening *in vitro* and *in vivo* to determine which compounds exhibit the desired pharmacological activities. There is no absolute predictability even in view of the seemingly high level of skill in the art. The existence of these obstacles establishes that the contemporary knowledge in the art would prevent one of ordinary skill in the art from accepting any therapeutic regimen on its face.

The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine whether or not all the claimed compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Thus, the specification fails to provide sufficient support of the broad use of the all the claimed compounds for the treatment of Down syndrome or Alzheimer disease. As a result, necessitating one of skill to perform an exhaustive search for which diseases can be treated by the claimed compounds in order to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, and 8-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claims 1, 8-13, the chemical terms " S-oxide thereof" is recited. These terms are vague and indefinite because the specification does not show the S-oxide of the claimed chemical compound in the examples which is different from the expression of X variable representing -SO- in the claims. The skilled artisan in the art claim is unable to figure out or predict what kind of the S-oxides of the claimed compounds. Therefore, an appropriate correction is required.

In claim 14-16, the term " medicament" is recited. This expression is vague and indefinite because this can be interpreted as a single drug or pharmaceutical

composition. The examiner recommends to change it to the pharmaceutical composition . Therefore, an appropriate correction is required.

In claims 15 and 16, the phrase " a medicament --- is used for treatment of a disease" is recited. This expression is vague and indefinite because of the hybrid claim which contains both pharmaceutical composition claim and method of treatment claim. The examiner recommends to separate it into two different claims. Therefore, an appropriate correction is required.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taylor Victor Oh whose telephone number is 571-272-0689. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Taylor Victor Oh/

Primary Examiner, Art Unit 1625

6/03/10